18th Annual scientific meeting of the Nederlandsche Vereniging voor Experimentele Dermatologie
2 and 3 February 2017

PROGRAMME

At the 18th annual scientific meeting of the NVED the ongoing scientific research in dermatology in the Netherlands will be presented.

PROGRAMME SUMMARY

Thursday 2 February 2017
09.30 - 10.15 Registration and welcome with coffee/tea
10.15 - 10.25 Opening by the chair of the NVED
10.25 - 11.55 Session I: Immunology and Infection
11.55 - 13.00 Lunch
13.00 - 14.30 Session II: Skin Biology and Skin Physiology
14.30 - 15.15 Poster and networking session I (with coffee/tea)
15.15 - 16.50 Session III: Gene mutation and Function
16.50 - 17.50 Guest Lecture by Prof. dr. Sara Brown (Dundee, Scotland, UK)
17.50 - 20.00 Drinks and Dinner
20.00 - 20.30 19th general assembly of the NVED

Friday 3 February 2017
09.00 - 10.15 Session IV: Clinical Studies
10.15 - 11.15 Poster and networking session II (with coffee/tea)
11.15 - 11.45 Guest Lecture by Prof. dr. Thomas Rustemeyer (VUmc)
11.45 - 13.00 Lunch
13.00 - 13.45 Session V: Dermato-Oncology
13.45 - 14.15 Guest Lecture by Prof. dr. Menno de Rie (AMC)
14.15 - 14.30 Break
14.30 - 15.20 Session V: Dermato-Oncology (continued)
15.20 - 15.30 Awards for best presentation and poster, selection breaking news
15.30 Closure

FULL PROGRAMME

THURSDAY 2 FEBRUARY 2017
09.30 - 10.15 Registration and welcome with coffee/tea
10.15 - 10.25 Opening by the chair of the NVED
10.25 - 11.55 Session I: Immunology and Infection

Session chairs: Errol Prens, Joost Schalkwijk
1. Tiago Matos AMC
   Identifying the T cell receptor sequences of pathogenic T cells of origin in psoriasis.
2. Dennis Hack AMC
   Biomarker analysis for disease severity and immunosuppressive treatment responsiveness in adult atopic dermatitis patients.
3. Danique van der Krieken RUMC The development of new Staphylococcus aureus-specific antibiotics.
5. Wim Zoutman LUMC Accurate quantification of T cells by measuring loss of germline T cell receptor loci with generic single duplex ddPCR assays in dermatological diseases.
6. Jos Smits RUMC Ligand and time dependent AHR activation: nuclear translocation and binding to genomic DNA.

11.55 - 13.00 Lunch

13.00 - 14.30 Session II: Skin Biology and Skin Physiology
Session chairs: Christianne Reijnders, Abdoel el Ghalbzouri

7. Rajiv Raktoe LUMC Exon skipping of TGFβRI affects signalling and ECM expression in hypertrophic scar-derived fibroblasts.
8. Taco Waaijman VUMC/ACTA Development of a vascularized skin equivalent for incorporation into an organ-on-chip device.
10. Hanneke Monsuur VUMC/ACTA Endothelial cells enhance scar characteristics in tissue-equivalents containing adipose-mesenchymal stromal cells.
11. Lenie van den Broek VUMC/ACTA Introduction of hair neopapillae into tissue-engineered skin.

14.30 - 15.15 Poster and networking session I (with coffee and tea)

P2. Withdrawn
P3. Annelies Lommerts AMC Autologous cell suspension grafting in segmental vitiligo and piebaldism: a randomized controlled trial comparing full-surface and fractional CO2 laser recipient site preparations.
P4. Selma Atalay RUMC Tight controlled dose reductions of biologics in psoriasis patients with low disease activity: a randomized pragmatic non-inferiority trial.
P5. Tiago Matos AMC The putative role of skin resident memory T cells in acute Graft-versus-Host-Disease.
P6. Rania Nabil LUMC Characteristics of patients at high risk for melanoma who return to the dermatology outpatient clinic for unscheduled visits.
P7. Maud Jansen MUMC Bowen’s Disease: Five-year results of Treatment with 5-Fluorouracil cream, Photodynamic Therapy and Surgical Excision.
P8. Janneke Kessels MUMC Topical Sinecatechin ointment for primary superficial basal cell carcinoma: can tea cure?
P10. Jart Oosterhaven UMCG Sickness presenteeism in a Dutch hand eczema population.
P11. Frederica Giurdanella UMCG In vitro keratinocytes binding test for pemphigus.
P13. Marisol Otero RUMC Methotrexate in patients with psoriasis, split for different reasons of discontinuation - Results of the prospective MTX-CAPTURE.
P14. Lieke van Vugt Predicting the response to biologics in patients with psoriasis through pharmacogenetics: a systematic review.

P15. Thalita Boldrin Zanoni Mixture used in permanent hair dyes enhances toxic effects in reconstructed 3D epidermal equivalents: Role of p-phenylenediamine, barrier loss and skin sensitization.


15.15 - 16.50 Session III: Gene mutation and Function
Session chairs: Ellen van den Bogaard, Hendri Pas

13. Eirini Christodoulou Using functional studies to explore a candidate high-penetrance melanoma susceptibility gene.
17. Jeroen Bremer Natural exon skipping in the COL7A1 gene paves the way for AON-mediated exon skipping for recessive dystrophic epidermolysis bullosa.
18. Hanna Niehues Late cornified envelope (LCE) proteins: a novel class of cutaneous host defense molecules.

16.50 - 17.50 Guest Lecture by Prof. dr. Sara Brown (Dundee, Scotland, UK):
‘The Molecular and Genetic mechanisms in Dermatology with a focus on new insights’

17.50 - 20.00 Drinks and Dinner

20.00 - 20.30 19th general assembly of the NVED

20.30 Social gathering

FRIDAY 3 FEBRUARY 2017

09.00 - 10.15 Session IV: Clinical Studies
Session chairs: Martijn van Doorn, Marjolein de Bruin

19. Louise Gerbens Methotrexate versus azathioprine in severe atopic dermatitis: A 5-year follow up study of a randomised controlled trial.
21. Inge Bronckers Data from an international pediatric psoriasis registry: use of methotrexate, reported adverse events and recommendations for folic acid prescription.
22. Judith Thijs Disease severity biomarkers in serum and dried blood spots from atopic dermatitis patients.
23. Mignon van den Elzen Effectiveness of omalizumab in a daily practice cohort of adults suffering chronic spontaneous urticaria.

10.15 - 11.15 Poster and networking session II, including poster walk and presentation of selected posters (with coffee and tea)

11.15 - 11.45 Guest Lecture by Prof. dr. Thomas Rustemeyer (VUmc):
Translational Contact Dermatitis: From Bench to the Clinic.

11.45 - 13.00 Lunch
13.00 - 13.45  **Session V: Dermato-Oncology**  
Session chairs: Marcel Bekkenk, Michel van Geel

24. Lotte van Lee  
*ErasmusMC*  
Complete excision and recurrence rates of squamous cell carcinoma after Mohs micrographic surgery or conventional excision.

25. Rania Nabil  
*LUMC*  
Comparison between a mobile phone application for the analysis of skin lesions and the clinical diagnosis of the dermatologist.

26. Nicolas Bastidas  
*LUMC*  
Whole-Genome Sequencing reveals recurrent DNA structural alterations in mycosis fungoides.

13.45 - 14.15  **Guest Lecture by Prof. dr. Menno de Rie (AMC):**  
‘Lost in translation’

14.15 - 14.30  **Break (stretch your legs)**

14.30 - 15.20  **Session V: Dermato-Oncology (continued)**

27. Safa Najidh  
*LUMC*  
Evaluation of validated DNA methylation biomarkers in suspected Sézary syndrome patients.

28. Suzanne van Santen  
*LUMC*  
Results of initial treatment in 203 Dutch patients with Folliculotropic Mycosis Fungoides.

29. Kim Nguyen  
*RUMC*  
Standard step sectioning of skin biopsies diagnosed as superficial basal cell carcinoma frequently yields deeper and more aggressive subtypes.

15.20 - 15.30  **Awards for best presentation and poster; selection breaking news**

15.30  **Closure**

**Meeting Location:**  
Congress hotel ‘De Werelt’  
Westhofflaan 2  
6741 KH Lunteren  
Tel: 0318-484641

**Accreditation:**  
The NVDV has awarded 11 points for full participation in this scientific meeting last year; accreditation for 2017 is applied for.

**Programme committee:**  

**Jury for presentation prize:**  
Frank de Gruijl (*LUMC*), Rosalie Luiten (*AMC*), Ewout Baerveldt (*ErasmusMC*)

**Jury for poster prize:**  
Mijke Visser (*LUMC*), Loes Hollestein (*ErasmusMC*), Patrick Jansen (*RUMC*)

**NVED board:**  
Phyllis Spuls (chair, AMC), Marieke Seyger (secretary, *RUMC*), Marjon Pasmooij (Treasurer, *UMCG*), DirkJan Hijnen (representative in NVDV, *UMCU*), Kees Tensen (representative in Federa, *LUMC*).
1. IDENTIFYING THE T CELL RECEPTOR SEQUENCES OF PATHOGENIC T CELLS OF ORIGIN IN PSORIASIS


1Department of Dermatology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA; 2Academic Medical Center, Department of Dermatology, University of Amsterdam, Amsterdam, 3Adaptive Biotechnologies, Seattle, WA, USA; 4Department of Dermatology, Rockefeller University, New York, NY, USA.

Background/Aim: Psoriasis is a uniquely human autoimmune disease mediated by IL-17 producing T cells. We studied non-lesional, lesional and previously lesional skin in patients who had cleared on etanercept therapy.

Results: We found expanded oligoclonal T cell populations in healed psoriatic lesions which produced IL-17 and/or IL-22 in active lesions from the same patients, suggesting they represent disease initiating T cells. Further alpha/delta TCR sequencing demonstrated that these putative disease initiating T cell clones were universally alphabeta T cells. In contrast to studies in mouse models, gammadelta T cells were rare in human psoriasis, previously lesional skin and in healthy human skin, making up only 1.6%, 0.45% % and 1.8% of the total T cell population respectively.

Discussion/Conclusion: By matching TCR alpha and beta sequences of initiating clones based on T cell frequency, we have obtained for the first time the complete TCR sequence of autoreactive T cells of origin in psoriasis. In short, we have identified for the first time the full TCR sequences of initiating T cells in psoriasis, the first step in future studies designed to identify the autoantigen in psoriasis.

2. BIOMARKER ANALYSIS FOR DISEASE SEVERITY AND IMMUNOSUPPRESSIVE TREATMENT RESPONSIVENESSNESS IN ADULT ATOPIC DERMATITIS PATIENTS

D.P. Hack3*, E. Roekevisch1, K. Szegedi1, M.E. Schram2, P.C.J.M. Res3, J.D. Bos1, M.M.G. Leeflang1, R.M. Luiten1, S. Kezic4, Ph.I. Spuls1, M.A. Middelkamp Hup1

3*Department of Dermatology, Academic Medical Center, University of Amsterdam, Amsterdam, 1Laboratory of Experimental Dermatology, Department of Dermatology, Academic Medical Center, University of Amsterdam, 2Coronel Institute of Occupational Health, Academic Medical Center, University of Amsterdam, Amsterdam

Background: Biomarkers to objectively measure disease severity and predict therapeutic responses are needed in AD.

Objective: To investigate a) correlations between circulating cytokine/chemokine profiles and AD severity parameters; b) differences between cytokine/chemokine profiles in AD patients responding and not responding to treatment with methotrexate (MTX) or azathioprine (AZA).

Methods: SCORAD, objective SCORAD, EASI, VAS-itch and VAS-sleep loss were measured in adult AD patients at baseline (n=43) and after 12 weeks of treatment (MTX n=19, AZA n=19). Serum levels of APRIL, BAFF, TARC (CCL-17), IL-1RA, IL-1β, IL-4, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-18, IL-31, IFN-γ, TNF-α, VEGF, MIG (CXCL-9), IP-10 (CXCL-10), MCP-1 (CCL-2), MIP-1β (CCL-4), RANTES (CCL-5), CTACK (CCL-27), TSLP, IL-5, IL-1α and G-CSF were analyzed by ELISA and Luminox, with 18 healthy volunteers as control. Responders to therapy were defined by a SCORAD reduction of ≥50%.

Results: CTACK levels significantly correlated (P≤0.0001) with SCORAD, objective SCORAD, and EASI at baseline; TARC showed no significant correlation. Serum levels of TARC, CTACK and VEGF showed a significant decrease after treatment with MTX and AZA, with no significant differences between both groups. No differences were found between responders and non-responders at baseline in cytokines/chemokines.

Conclusion: Serum CTACK may be a biomarker for disease severity in AD patients, requiring further analysis. Serum levels of TARC, CTACK and VEGF significantly decreased upon treatment with MTX and AZA, but none of the cytokines/chemokines measured could predict a therapeutic response.

3. THE DEVELOPMENT OF NEW STAPHYLOCOCCUS AUREUS-SPECIFIC ANTIBIOTICS


Department of Dermatology, Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Nijmegen

Background: Staphylococcus aureus is a frequent cause of cutaneous infections. More than 80% of atopic dermatitis (AD) patients is colonized by...
S. aureus. The increasing evidence for a role of S. aureus in AD suggests that S. aureus-specific antibiotics may be of therapeutic value. The emerging resistance of S. aureus against current antibiotics calls for the development of novel anti-Staphylococcal therapies. Preferably these antibiotics should target only S. aureus and not the commensal microbiome. The pantothenamide class of antibiotics has been described to target coenzyme A biosynthesis of Gram-positive bacteria, but we have recently discovered that these pantothenamides were prone to enzymatic degradation, making them unsuitable for clinical application. We here describe the synthesis and antibiotic activity of novel pantothenamides that were chemically stabilized against degradation.

**Methods:** Pantothenamides were obtained by synthetic organic chemistry and their stability in vitro and in vivo was determined by LC-MS. The antibiotic activity was determined in antimicrobial assays. A cell-free skin infection model was used to test topical administration.

**Results:** Pantothenamides were modified by inverting the susceptible amide bond. These inverted amides were found to be stable in human serum in vitro, and in vivo in rats. Some of the compounds are particularly interesting as they were active against S. aureus, but less against commensal skin bacteria.

**Conclusion:** Our data suggest that inverted pantothenamides are a promising new class of Staphylococcus-specific antibiotics for topical use. Targeted treatment of S. aureus colonization without altering the commensal bacterial community, could be beneficial in the treatment of skin diseases like AD.

### 4. RESPONSE OF GINGIVA EQUIVALENTS TO COMMENSAL AND PATHOGENIC ORAL MICROBIOMES

J.K. Buskermolen¹, M.M. Janus², B.P. Krom³, S. Gibbs⁴

*Department of ¹Oral Cell Biology and ²Preventive Dentistry, Academic Centre for Dentistry Amsterdam, University of Amsterdam, and VU University Amsterdam, MOVE Research Institute Amsterdam, ³Department of Dermatology, VU University medical center, Amsterdam*

**Introduction:** Host-microbiome interactions play an important part in regulating human health. Microbiomes consist of up to 200 different species of bacteria. Whereas commensal oral microbiomes do not damage the host tissue, pathogenic oral microbiomes cause diseases such as gingivitis or caries.

**Aim:** The aim of this study was to determine the host response to commensal and pathogenic oral microbiomes with the aid of full thickness tissue engineered gingiva equivalents (GE).

**Methods:** The GE consisted of a fully differentiated epithelium on a fibroblast populated collagen hydrogel. Three distinct oral microbiomes were grown, resembling a commensal, gingivitis and cariogenic phenotype. GE were exposed to the microbiomes for 24 hours. GE response to the different microbiomes was analyzed by histology and inflammatory mediator release (ELISA).

**Results:** A dense layer of commensal, gingivitis or cariogenic bacteria were observed on GE tissue sections. Commensal and cariogenic bacteria had no detrimental effects on GE histology. However gingivitis bacteria caused a disruption in tissue integrity in the upper epithelial layers. Notable differences were observed in the secretion of inflammatory cytokines. IL-6, CXCL8 and CCL20 secretion was higher when the GE were exposed to commensal microbiomes than to pathogenic microbiomes. In contrast, CCL5 upregulation was similar for all three microbiomes.

**Conclusions:** Commensal microbiomes and pathogenic microbiomes induce a different inflammatory cytokine response in gingiva tissue. Notably, GE secreted higher amounts of pro-inflammatory cytokines in response to the commensal microbiome than in response to the pathogenic microbiome. Our results indicate that the pathogenic microbiome might actively evade the immune response.

### 5. ACCURATE QUANTIFICATION OF T CELLS BY MEASURING LOSS OF GERMLINE T CELL RECEPTOR LOCI WITH GENERIC SINGLE DUPLEX DDPCR ASSAYS IN DERMATOLOGICAL DISEASES

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**Background:** A major compartment of the immune cell repertoire in skin is occupied by T cells. Moreover, the presence of infiltrating T cells in dermatological diseases is relevant with respect to diagnostics, prognostics and therapeutic approaches. Quantifying T cells in benign, inflammatory or malignant specimens can be of great importance for a variety of clinical conditions in dermatology accordingly. Immunohistochemistry and flow cytometry are accustomed techniques for quantification. However, these methods require fresh, frozen or fixed specimens.

**Method:** We alternatively developed and validated generic droplet digital (dd)PCR assays to quantify T cells accurately in DNA samples. Furthermore, these assays have been utilised to quantify peripher al T cells in Sézary syndrome (SS) and tumour infiltrating T cells in uveal melanoma (UM). DNA was extracted from skin derived fibroblasts, peripheral blood from SS patients, healthy donors and from UM tumour samples.


Results: By measuring loss of germline Dδ2-Dδ3 and/or Dβ1-Dβ2 intergenic T-cell receptor (TCR) sequences with ddPCR we were able to quantify (infiltrating) T cells in a variety of DNA samples.

Discussion: We found it to be as accurate as gold-standard methods of quantification. Measuring loss of germline TCR loci by using ddPCR is a novel and sensitive method for quantifying T cells relatively fast, accurate and independent of the cellular context. Since ddPCR requires small amounts of DNA instead of freshly isolated, frozen or fixated cells and tissue, the sample size and variety of initially unanalyable and/or scarce material for quantifying (infiltrating) T cells in cutaneous diseases can be expanded significantly.

6. LIGAND AND TIME DEPENDENT AHR ACTIVATION: NUCLEAR TRANSLLOCATION AND BINDING TO GENOMIC DNA

J.P.H. Smits1, J. Qu1, P.L.M. Zeeuwen1, J. Schalkwijk1, H. Zhou1,2, E.H. van den Bogarda1
1Department of Dermatology, Radboud Institute for Molecular Life Sciences (RIMLS), Radboud University Medical Center (Radboudumc), 2Department of Molecular Developmental Biology, RIMLS, Faculty of Science, Radboud University, 3Department of Human Genetics, RIMLS, Radboudumc, Nijmegen

Background: The therapeutic effect of coal tar treatment in atopic dermatitis is mediated via aryl hydrocarbon receptor (AHR) activation. The AHR is a multifaceted transcription factor involved in xenobiotic metabolism, immune cell development, and epidermal differentiation. For a better understanding of the AHR ligand promiscuity that results in severe toxicity by dioxin-like compounds but therapeutic effects by coal tar, we studied the ligand-mediated DNA binding of the AHR and its target gene transcription in keratinocytes.

Methods: Human primary keratinocytes treated with TCDD or coal tar were subjected to chromatin immunoprecipitation followed by whole genome deep-sequencing (chip-seq) and quantitative PCR to study genome-wide AHR binding and target gene regulation, respectively.

Results: We first analyzed the time dependent AHR binding to known target genes and we detected AHR binding to CYP1A2 already after 30 minutes of coal tar and TCDD exposure. Chip-seq analysis indicated that after 30 minutes, the AHR is mainly bound to promoter regions of genes involved in detoxification pathways with great overlap between both treatments. Only a few, yet undefined, genes were solely bound by coal tar-activated AHR.

Discussion: Our study indicates that the AHR binds to similar regions on the genome in the first response to TCDD and coal tar and that cellular responses are initially directed towards activation of xenobiotic metabolism pathways. We therefore hypothesize that the differences in health outcome after TCDD and coal tar exposure is due to seconda-ry responses at a later time point of AHR activation, which will be subject of further research.

7. EXON SKIPPING OF TGFRI AFFECTS SIGNALLING AND ECM EXPRESSION IN HYPERTROPHIC SCAR-DERIVED FIBROBLASTS

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Introduction: In burn patients wound healing is often accompanied by hypertrophic scar (HTS) development, resulting in both functional and aesthetic problems. HTS’s are characterized by abundant presence of myofibroblasts, which contribute to excessive production of extracellular matrix (ECM) components. The TGF-β signalling pathway plays a key role in the differentiation and activity of the myofibroblasts. Previous studies have shown that inhibition of TGF-β receptors in fibrotic diseases, such as Dupuytren’s disease, results in a significant reduction of the fibrotic load. In this study we have investigated the effects of exon skipping using antisense oligonucleotides (AON’s) to inactivate Alk5 (TGF-β receptor 1) in HTS-derived fibroblasts.

Methods: HTS biopsies were used to set up fibroblast monocultures. In order to induce exon skipping, AONs targeting Alk5 were supplemented to fibroblast monocultures. Chemical inhibition was performed with the Alk5 inhibitor SB431542. Validation of AON delivery in monocultures was performed with immunofluorescence. Analysis of TGF-β signalling downstream targets, collagens and migration was performed by qPCR, touchdown PCR and microscopy.

Results: Our data demonstrate that 1) AONs are delivered in HTS-derived fibroblasts, 2) exon skipping of Alk5 was successful, 3) exon skipping affects the expression of ECM-related genes in monolayers of HTS-derived fibroblasts, and 4) AON treatment affects the migration of fibroblasts during wound healing.

Conclusion: In conclusion, exon skipping is a promising tool in order to modulate the TGF-β signaling pathway and, thereby, the expression of ECM components in HTS. This would open a therapeutic window for the treatment of HTS patients.

8. DEVELOPMENT OF A VASCULARIZED SKIN EQUIVALENT FOR INCORPORATION INTO AN ORGAN-ON-CHIP DEVICE

T. Waaijman1, L. Berghs1, S. Gibbs1
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Introduction: Skin Equivalents (SE) generally consist of a reconstructed epidermis on a fibroblast populated dermal matrix. Endothelial cells which form an important part of the vasculature are missing. In order to develop more advanced skin models for incorporation into organ-on-chip devices it is important to introduce endothelial cells and to determine the influence of these cells on inflammatory signals regulating migration of immune cells into and out of SE. The aim of this study was to determine the influence of a confluent layer of endothelial cells beneath the SE on inflammatory chemokine secretion.

Methods: SE were constructed from healthy adult skin. Endothelial cells were isolated from dermis and consisted of >98% CD31+ cells. Passage 6-9 cells were seeded on the underside of the transwell and cultured for 3 weeks. SE were harvested for tissue architecture and assessed by immunohistochemistry; inflammatory mediator secretion was assessed by ELISA.

Results: A confluent layer of CD31+ endothelial cells was observed covering the underside of the transwell. SE showed normal epidermal differentiation with proliferating Ki67-keratinocytes in the basal layer and Keratin-10 expression in suprabasal layers. Notably, SE with endothelial cells secreted lower amounts of inflammatory mediators (IL-8, CCL-5, CCL-2, IL-6, CCL-27 and CXCL-12) which are responsible for recruitment or emigration of immune cells compared to SE without endothelial cells.

Conclusions: Endothelial cells suppress inflammatory signals from SE which needs to be taken into account when developing immune competent skin-on-a-chip models. Our results illustrate the crosstalk which occurs in skin between keratinocytes, fibroblasts and endothelial cells.

9. AN IN VITRO STUDY TO DETERMINE THE WOUND HEALING POTENTIAL OF HUMAN SALIVA


Materials and Methods: Human saliva was collected from healthy volunteers and filter sterilized before adding to cell cultures. Skin and oral fibroblast migration was assessed using a scratch assay. Skin and oral mucosa tissue equivalents were used to assess epithelial differentiation, re-epithelialization and inflammatory mediator secretion, after introduction of full thickness wounds.

Results: Saliva stimulates migration of skin and oral mucosal fibroblasts. It stimulated faster re-epithelialization in oral-mucosa equivalents than in skin equivalents without influencing normal differentiation. Notably, saliva promoted an innate inflammatory response (increased CCL20, IL-6 and CXCL-8 secretion) in both skin and oral-mucosa wounded equivalents.

Discussion/conclusion: Our results show that human saliva has the potential to stimulate skin wound closure and an inflammatory response. Inflammation is required to drive wound healing and tissue remodelling. Further research aims to determine whether a saliva therapy can be developed for skin wound healing.

10. ENDOTHELIAL CELLS ENHANCE SCAR CHARACTERISTICS IN TISSUE-EQUIVALENTS CONTAINING ADIPOSE-MESENCHYMAL STROMAL CELLS

H.N. Monsuur, L.J. van den Broek, F.B. Niessen, P. Koolwijk, S. Gibbs

Background: Hypertrophic scars (HS) are often formed after 3rd degree burn wounds where adipose tissue is exposed. Previously, we have shown with the aid of human skin equivalents that mesenchymal stromal cells isolated from the adipose tissue (adipose-MSC) most probably contribute to HS formation. The role of endothelial cells in HS formation has not yet been investigated even though HS typically have a higher vascular density compared to normotrophic scars.

Aim: To determine whether endothelial cells influence HS characteristics in tissue-equivalents constructed with adipose-MSC or dermal-fibroblasts.

Method: Dermal-fibroblasts or adipose-MSC were seeded into a collagen-elastin matrix alone or in combination with dermal- or adipose-derived endothelial cells. Contraction was measured, immunohistochemistry was performed to detect endothelial cells (CD31 staining) and myofibroblasts (α-SMA staining), and soluble factors associated with fibrosis were assessed by ELISA.

Results: Tissue-equivalents with endothelial cells all contained small vascular structures. Endothelial
cells, independent of their origin (dermal or adipose) enhanced contraction, a typical HS characteristic, only in tissue-equivalents containing adipose-MSC (but not dermal-fibroblasts). The enhanced contraction could not be explained by the presence of myofibroblasts as α-SMA was absent. Secretion of anti-fibrotic factor HGF was less in tissue-equivalents containing adipose-MSC compared to those containing dermal-fibroblasts and was not further influenced by endothelial cells. In contrast, secretion of anti-fibrotic factor Follistatin which also showed decreased secretion in adipose-MSC tissue-equivalents, was substantially further decreased when endothelial cells were present.

Conclusion: Endothelial cells result in enhanced contraction and decreased Follistatin secretion by adipose-MSC and thus may contribute to scar formation.

11. INTRODUCTION OF HAIR NEOpAPILLAE INTO TISSUE-ENGINEERED SKIN

L.J. van den Broek1,2, M. Thon1,2, B. Atac1,4 G. Lindner3, U. Marx3, S. Gibbs1,5
1Department of Dermatology, VU University Medical Center, Amsterdam, 2A-Skin BV, Amsterdam, 3Technical University Berlin, Institute of Biotechnology, Berlin, Germany, 4TissueUse GmbH, Berlin, Germany, 5Department of Biochemistry, Academic Center for Dentistry Amsterdam, University of Amsterdam and VU University, Amsterdam

Background/Aim: Tissue-engineered skin constructs are used to treat skin wounds and to test safety and efficacy of actives. Although current skin constructs mimic the human skin to a certain extent, they do not contain appendages like hair follicles. The aim of this study was introduce hair neopapillae into tissue-engineered skin constructs.

Methods: Dermal papilla cells were isolated from human hair follicles from the scalp and expanded. Expanded dermal papilla cells were used to construct neopapillae (spheroids of dermal papilla cells). Neopapillae were introduced into skin constructs with a reconstructed epidermis containing keratinocytes and melanocytes on a fibroblast populated hydrogel. After introduction of neopapillae, skin constructs were cultured for 7 to 21 days.

Results: Neopapillae were observed in skin constructs up to 21 days of culture. Epidermis of skin constructs showed normal differentiation with a stratum corneum. Neopapillae were located within the hydrogel directly in contact or close to the epidermis and stayed compact during culture. Epidermal cells can be seen growing towards and enclosing the neopapillae.

Conclusion: Neopapillae could be introduced and maintained in skin constructs. They stayed compact and became enclosed by epidermal cells. This is the first stage towards creating viable hair in skin equivalents. Such constructs are required for in vitro testing platforms and human hair transplantation.

12. UTILIZATION OF NATIVE HUMAN COLLAGEN IN FULL THICKNESS HUMAN SKIN MODELS DOES NOT ALTER EPIDERMAL BARRIER FORMATION

A. Mieremet1, M. Rietveld1, R. van Dijk2, J.A. Bouwstra2,3, A. El Ghalbzouri
1Department of Dermatology, Leiden University Medical Centre, 2Division of Drug Delivery Technology, LACDR, Leiden University
3Senior authors contributed equally to this work

Background: The major limitation of reconstructed human skin models is the higher permeability for compounds, when compared to native human skin (NHS). Alterations in the lipid matrix of the stratum corneum (SC) highly contribute to this occurrence. The dermal matrix of the current full thickness models (FTMs) consists of rat-tail tendon collagen populated with fibroblast. In this study we aim to mimic the in vivo skin to a higher extent in the FTMs, through replacement of rat-tail tendon collagen for native human collagen.

Materials and Methods: An isolation procedure to obtain soluble collagen from human abdominal dermis was developed. Subsequently, FTMs and human collagen full thickness models (hC-FTMs) were generated. Immunohistochemical analyses were performed to obtain insight in dermal and epidermal homeostasis. The SC ceramide composition was studied with liquid chromatography combined with mass spectroscopy. Lipid lamellar organization was examined by small angle X-ray diffraction.

Results: The FTMs and hC-FTMs exhibit many similarities, including the dermal matrix structure, basement membrane formation, basal layer proliferation and execution of the differentiation programs. The epidermal barrier of both FTM types contained similar number of corneocyte layers and equal level of lipids. The ceramide chain length distribution and ceramide subclass profile only showed minor differences, which resulted in an unaltered lamellar organization.

Conclusion: This study shows that animal-free hC-FTMs can be generated successfully. Despite the utilization of human collagens in the in vitro developed skin model, epidermal and dermal morphogenesis and lipid barrier formation do not resemble that of NHS to a higher extent.

13. USING FUNCTIONAL STUDIES TO EXPLORE A CANDIDATE HIGH-PENETRANCE MELANOMA SUSCEPTIBILITY GENE

1Department of Dermatology, Leiden University Medical Centre
2Queensland Institute of Medical Research, Herston, Australia
Background: Melanoma is the most aggressive type of skin cancer. Almost 10% of patients have family history of melanoma. Familial melanoma is defined as development of melanoma in at least three members of a family, two of which are first degree relatives. Mutations in CDKN2A and other genes are known to cause familial melanoma; however the genetic basis of over half of the cases remains to be clarified.

Aim: The aim of this project is to functionally characterise a newly identified high-penetration melanoma susceptibility gene.

Results: In a collaborative exome sequencing study, we identified a germ-line nonsense mutation in the NEK11 gene (R374X) in all five affected members of a family, resulting in a truncated protein formation. NEK11 is a plausible candidate melanoma-predisposition gene given its role in the G2/M cell cycle checkpoint. Following DNA damage, NEK11 protein is activated, resulting in phosphorylation and ubiquitin-mediated degradation of CDC25A, which in turn prevents progression to M phase allowing DNA repair. Functional inactivation of NEK11 could bypass DNA damage-induced cell repair ability by disrupting G2/M arrest. Here, we show that wild-type (WT) NEK11 assists in CDC25A ubiquitination upon co-expression in U-2 OS cells. Expression of mutant NEK11 was associated with decreased CDC25A ubiquitination when compared to WT.

Discussion/conclusion: Gorlin patients treated with Vismodegib can develop resistant BCCs due to the development of specific SMO mutations within their tumors. Genetic profiling of (resistant) BCCs may be used as diagnostic tool to personalize BCC treatment.

15. DISSECTING HUMAN EPIDERMAL COMMITMENT OF HUMAN INDUCED PLURIPOTENT STEM CELLS IN HEALTH AND DISEASE

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Ectodermal dysplasia represent different syndromes affecting development of skin and ectodermal derived structures. Among these syndromes, the ones caused by mutations on the transcription factor p63 show striking developmental defects. For example, ectrodactyly, ectodermal dysplasia, cleft lip/plate syndrome (EEC) patients show abnormalities on skin development. Here, we established a reproducible and robust protocol to recapitulate human epidermal commitment under feeder-free conditions to compare transcriptional changes driving normal and diseased epidermal development. In order to gain insights on cell-to-cell variation that may be important for the developmental outcome we performed RNA-seq at single cell resolution the described system for normal and diseased epidermal commitment of hiPSCs and compared with the human primary keratinocytes. By bulk RNA-seq of the wild type cell line we noticed strong molecular similarities between iPSC derived keratinocytes (iKeratinocyte) and human primary keratinocytes. Immunostaining and qPCR analyses of lineage-specific markers confirmed the genome-wide analysis. In addition, normal iKeratinocytes are able to stratify in vitro, as we seen by up-regulation of supra
basal epithelial markers such as TG1, Involurin and Cysme, after stratification induction in 2D. In the other hand, p63 mutant cell lines P63 show expression of simple epithelium markers but fail to express epidermal genes. RNA-sequencing analyses are being carried out at moment in order to compare the transcriptomes of p63 mutant cell lines in relation to the normal using bulk and single cell RNA-sequencing. Our preliminary data shows that proper p63 expression is essential for normal epidermal commitment of hiPSCs.

16. ENHANCER-DRIVEN TRANSCRIPTIONALREWIRING CAUSED BY P63 MUTATIONS INEEC SYNDROME LEADS TO LOSS OF PROPER EPIDERMAL CELL FATE

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Background: During epidermal development and stratification, the transcription factor p63 functions as a master regulator. Heterozygous point mutations in p63 cause a spectrum of developmental disorders, among which mutations in the DNA binding domain lead to ectodactyly, ectodermal dysplasia, cleft lip/palate (EEC) syndrome.

Method: Using a well-established in vitro model recapitulating in vivo epidermal stratification, epigenomic profiling of the promoter mark H3K4me3, the active enhancer mark H3K27ac and the repressive mark H3K27me3 as well as RNA-Seq analyses have been performed in patient keratinocytes carrying p63 EEC mutations to obtain an overview of epigenetic mechanism in EEC syndrome.

Results: RNA-Seq revealed 7968 differentially expressed genes in patient keratinocytes in comparison with control keratinocytes with down-regulated epidermal and up-regulated non-epidermal genes, which suggests that p63 mutant keratinocytes have less defined epidermal identity. Further characterization of p63 binding in combination with histone modifications showed that mutations in p63 DNA binding domain can result in genome-wide decrease of p63 binding and a redistribution of H3K27ac and H3K27me3. Whereas loss of p63 binding results in loss of the active enhancers, motif prediction showed that abnormal recruitment of co-regulating transcription factors of p63 may induce gained enhancers, thus activating genes that should not express in normal keratinocytes.

Discussion/Conclusion: Taken together, our data indicate that transcription rewiring occurs in p63 mutant keratinocytes, which may lead to less defined epidermal identity of the epidermal cells and contribute to the epidermal phenotype of the disease. Gene mutation and function

17. NATURAL EXON SKIPPING IN THECOL7A1 GENE PAVES THE WAY FOR AON-MEDIATED EXON SKIPPING FOR RECES SIVE DYSTROPHIC EPIDERMOLYSIS BUL-LOSA

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Dystrophic epidermolysis bullosa (DEB) is a devastating blistering disease affecting skin and mucous membranes. The disease is caused by mutations in the COL7A1 gene, which encodes type VII collagen (C7), and can be inherited dominantly or recessively. The extracellular C7 aggregates to form anchoring fibrils that secure attachment of the epidermis to the dermis. The disease severity is highly correlated to the quality and quantity of residual C7 expression. Our current focus of research lies on antisense oligonucleotide-mediated exon skipping as therapeutic approach for DEB. The precise therapeutic gain to be anticipated is currently unclear. Studying patients in which COL7A1 mutations cause natural exon skipping, would shed light on the potential of AON-mediated exon skipping as therapeutic approach for DEB. We present a case series of patients carrying mutations that lead to natural exon skipping. Molecular analyses were performed on DNA, RNA, and protein level, to gain insight into the genotype-phenotype correlation of exon skipping in DEB. To complete the genotype-phenotype correlation, the Dutch EB registry was scrutinized for exon skipping mutations and the pertinent literature on this class of mutations was reviewed. Exon skipping can effect in both a dominant and recessive manner. In dominant exon skipping cases, the phenotype cannot be distinguished from other dominant DEB phenotypes, for example a single glycome substitution. In recessive exon skipping cases, the phenotype is relatively mild in the phenotypic spectrum of recessive DEB. Therefore, exon skipping would be most beneficial for severe recessive DEB, and not for dominant DEB.

18. LATE CORNIFIED ENVELOPE (LCE) PROTEINS: A NOVEL CLASS OF CUTANEOUS HOST DEFENSE MOLECULES

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HOST DEFENSE MOLECULES: A NOVEL CLASS OF CUTANEOUS HOST DEFENSE MOLECULES

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Background/aim: Late cornified envelope (LCE) genes encode a family of 18 keratinocyte-expressed proteins located in the epidermal differentiation complex (EDC) on chromosome 1. Deletion of LCE3B and LCE3C (LCE3B/C-del) is a widely replicated psoriasis risk factor, but the function of LCE proteins, and consequently, the biology underlying the risk conferred by this genetic signal is unknown.

Materials/methods: To investigate the effect of LCE3B/C-del on expression of nearby genes, we performed cis-expression quantitative trait locus analysis for genes spanning the EDC, utilizing RNA-seq data from skin biopsies and the psoriasis-associated SNP rs4112788 as a proxy for LCE3B/C-del. We then investigated the function of the LCE3A, LCE3B and LCE3C with respect to skin barrier and host defense.

Results: The rs4112788 risk allele was associated with a significant, 12-fold increase in expression of LCE3A, most likely due to genomic effects of the deletion. Of all LCE genes, particularly LCE3A was significantly induced by keratinocyte exposure to TLR ligands. Regarding barrier function, we found that LCE3B/C-del did not influence epidermal permeability for low molecular weight tracers and water. Most importantly, we discovered that LCE3 proteins, have broad spectrum antimicrobial activity against gram-positive and gram-negative bacteria at low micromolar concentrations.

Discussion/conclusion: We have shown that the LCE3B/C-del psoriasis risk locus comprises more than just a loss of two proteins; it also affects the neighbouring LCE3A gene. We, for the first time identify a biological function for LCE3 proteins and we suggest a central role of LCE3A in the mechanism of LCE3B/C-del mediated psoriasis risk.

19. METHOTREXATE VERSUS AZATHIOPRINE IN SEVERE ATOPIC DERMATITIS: A 5-YEAR FOLLOW UP STUDY OF A RANDOMISED CONTROLLED TRIAL

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Background: Systemic treatment is indicated for moderate-to-severe atopic dermatitis (AD), refractory to topical treatment. Long-term evidence, up to 5 years, of off-label prescribed methotrexate (MTX) and azathioprine (AZA) is lacking.

Objectives: To investigate the long-term efficacy, safety and drug survival of MTX and AZA.

Methods: In an open-label follow up phase of a clinical trial patients were seen every 3 months for 5 years. MTX and AZA doses could be increased as in daily clinical practice. Primary efficacy outcomes were the mean absolute and relative reduction in SCORing Atopic Dermatitis (SCORAD) index and Investigator Global Assessment (IGA) after 5 years compared to baseline. For safety the type, frequency, severity and relatedness to treatment of adverse events were investigated. Drug survival was analysed by Kaplan-Meier curves.

Results: Thirty-five of 43 originally included patients participated, of which 27 completed follow up. At year 5 the mean relative reduction in SCORAD index was similar in MTX and AZA group; 56.9% vs. 60.1% (P=0.420) by intention-to-treat analysis and 52.8% vs. 53.8% by descriptive analysis. Seventy-eight adverse events were reported as most likely related to study medication; 36 for MTX and 42 for AZA. Eleven serious adverse events occurred during 5 years; for three a causal relationship could not be excluded. Drug survival demonstrated a significantly longer survival for MTX compared to AZA (P=0.03).

Conclusion: Based on this relatively small study, no difference can be observed in efficacy and safety between MTX and AZA as maintenance treatments in moderate-to-severe AD after 5 years.

20. LONG-TERM OUTCOME MEASURES IN EOSINOPHILIC FASCIITIS: A CROSS-SECTIONAL EVALUATION

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Background: Eosinophilic fasciitis (EF) is a rare connective tissue disorder. Debilitating skin fibrosis and consequential joint contractures can lead to functional and mental impairment. The disease is regarded self-limiting and disease remission is often achieved within a couple of years with or without treatment. However, irreversible damage can develop, and may impact the quality of life severely in the years following disease remission. Overall, little is known about the long-term behavior and impact of this uncommon condition.
Aim: The primary objectives were to evaluate the presence of disease activity and severity of damage during the course of the disease using clinical and patient reported outcome measures. Methods: A cross-sectional study of histopathological proven EF patients was conducted. The following outcome measures were assessed: LoSCAT, PhysGA-Activity, PhysGA-Damage, mRSS, mSS, and passive range of motion (ROM). In addition, patient reported outcomes consisted of PatGA-Score, PatGA-Damage, DLQI, SF-36, and HAQ. Results: In total, 32 EF patients (21 females, 65.6%), aged 27 to 78 years at study participation, were included. Two-thirds (N=22, 68.8%) of the patients had minimally active disease (PhysGA-Activity ≥5). However, we observed irreversible damage in 75% of the patients (PhysGA-Damage ≥5). Preliminary subanalysis showed that age at disease onset correlated with PatGA-damage and PhysGA-damage scores (Spearman r=0.48, p=0.0046 and Spearman r=0.1846, p=0.0126). Conclusion: In contrast with literature, irreversible damage was frequently present in EF patients. As age of disease onset correlates with the severity of the irreversible damage, older patients with EF could require additional care to prevent this irreversible damage.

21. DATA FROM AN INTERNATIONAL PEDIATRIC PSORIASIS REGISTRY: USE OF METHOTREXATE, REPORTED ADVERSE EVENTS AND RECOMMENDATIONS FOR FOLIC ACID PRESCRIPTION

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Background/Aim: Little is known about adverse events (AEs) in MTX-treated pediatric psoriasis patients. We aimed to investigate the occurrence of AEs in this population and the role of folic acid regimen. In Europe folic acid administration once weekly is common practice.


Results: 270 pediatric patients were treated with MTX (127 males). Mean age at diagnosis was 8.4 ± 3.6 and age at initiation of systemic treatment was 11.5 ± 3.6. Of these patients, 130 (48.1%) reported 1 or more AEs related to MTX, of which 67 (51.5%) were gastrointestinal (GI). Three patients (1.1%) developed a serious AE. Folic acid was prescribed in 239 (85.2%) patients using 3 regimens, each in 1/3 of patients: once weekly vs. 7 days/wk vs. 6 days/wk avoiding the MTX day. The occurrence of 1 or more AEs overall was not statistically different among folic acid regimens, but a GI AE was more common with weekly (43.7%) vs. daily (16.2%) or 6 day/wk (16.5%) folic acid (P<0.001) corrected for treatment duration. The efficacy of MTX after 6-months’ treatment did not differ between groups, with a tendency towards a decreased efficacy with folic acid 7 days/wk.

Conclusion: In this population, gastrointestinal AEs most frequently occurred from folic acid once weekly. These results suggest the introduction of a change in folic acid prescription practice in Europe from once weekly to 6 days/wk in pediatric psoriasis patients.

22. DISEASE SEVERITY BIOMARKERS IN SERUM AND DRIED BLOOD SPOTS FROM ATOPIC DERMATITIS PATIENTS

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Background: The number of trials evaluating new biologicals for atopic dermatitis (AD) is steadily increasing. Objective biomarkers are essential for study comparability and better identification of patients that benefit from these treatments. In a recent pilot study we showed that a panel of biomarkers is more suitable for assessing disease severity than a single biomarker. We also showed that measurement of biomarkers in dried blood spots (DBS) - drops of capillary blood collected from fingerprick - represent a minimally invasive alternative to serum biomarkers.

Aim: Validate and optimise a panel of biomarkers for measuring disease severity in serum and DBS from AD patients.

Materials/Methods: In a prospective cohort study 65 AD and 17 psoriasis patients were followed-up approximately 3 months. 27 non-atopic controls were included. Disease severity was assessed by EASI, POEM and VAS pruritus in AD patients, and PASI and SA-PASI in psoriasis patients. The biomarkers IL-1α, IL-2, IL-31, TARC, PARC, MDC sIL-2R, sE-selectin, SDF-1α and I309 were measured in serum and DBS.

Results: A mixed model analysis revealed significant correspondence of serum IL-1α, IL-2, TARC, MDC, and I309 with EASI scores in AD patients. Levels were significantly higher in AD compared to controls. Serum biomarker levels in psoriasis patients remained stable during follow-up. Biomarker levels in DBS were comparable to levels in serum.

Conclusion: A panel of biomarkers including IL-1α, IL-2, TARC, MDC, and I309 is more suitable for assessing disease severity than a single biomarker in
AD patients. Moreover, DBS offer a minimally invasive alternative for biomarker measurement.

23. EFFECTIVENESS OF OMALIZUMAB IN A DAILY PRACTICE COHORT OF ADULTS SUFFERING CHRONIC SPONTANEOUS URTICARIA

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Background: Efficacy and safety of omalizumab is proven in chronic spontaneous urticaria (CSU), but in randomized controlled studies only data up to 6 months of treatment are available. Patients in clinical trials differ from daily practice patients. We assessed the effectiveness of omalizumab in adult CSU patients in daily practice.

Methods: A monocenter prospective cohort study was performed. Patient-reported outcomes investigated effectiveness, defined as an urticaria control test (UCT) score %, Demographics, disease characteristics, side effects and (concomitant) treatment regimens were retrieved from patient records.

Results: Fifty-two patients were treated with a median of 11 omalizumab administrations (range 4-38). Thirty-seven (71%) were treated with antihistamines higher than fourfold, and 37 (71%) with immunosuppressants. History of atopy was reported in 23 (44%). Omalizumab was effective in 49 patients (94%) after a median of 1 administration (range 1-5). Intervals between omalizumab administrations were successfully elongated in 31 patients (61%), 4 (8%) stopped omalizumab after achieving remission. Exacerbations, defined as UCT <12, were observed in 30 (58%). In 10 patients (19%) omalizumab was up-dosed or the interval was shortened yielding effectiveness in 2. Side effects including headache, dizziness, malaise, fatigue, and hair loss, were reported by 38 (73%), in 18 (37%) at no more than three administrations. Five patients (10%) discontinued omalizumab due to side effects.

Conclusion: Omalizumab was highly effective (94%). However, a majority experienced exacerbations. Doses and intervals could be adjusted individually. Side effects occurred in a majority, and were only in a minority a reason for discontinuation of treatment.

24. COMPLETE EXCISION AND RECURRENCE RATES OF SQAMOUS CELL CARCINOMA AFTER MOHS MICROGRAPHIC SURGERY OR CONVENTIONAL EXCISION

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Background: Gold standard of treatment for cutaneous squamous cell carcinomas excision. Mohs micrographic surgery is considered as an alternative for excision for high risk squamous cell carcinoma.

Objective: Determine differences between excision and Mohs surgery in complete excision and recurrences of squamous cell carcinoma in the head and neck area.

Methods: Retrospective case series of all squamous cell carcinoma located in the head and neck area which were treated with excision or Mohs surgery at the departments of Dermatology at Erasmus University Medical Centre or Isala Hospital between 2003 and 2012. Pathology files were analysed to detect incompletely excised squamous cell carcinoma. To detect all recurrences, patients were linked to The nationwide network and registry of histo- and cytopathology (PALGA).

Results (preliminary): In total, 780 squamous cell carcinoma were included of which 360 were treated with excision and 420 with Mohs surgery. Squamous cell carcinoma were more often completely excised with Mohs surgery (99%) than with excision (94%, p<0.005). Mean follow-up was 20 months for Mohs surgery (standard deviation 16.9) and 38 months for excision (standard deviation 27.2, p<0.005). After Mohs surgery, squamous cell carcinoma recurred less often (3%) than after excision (7%, p<0.005), while with Mohs surgery more high risk squamous cell carcinoma were treated (12.6%) than with excision (10.3%, p<0.05).

Conclusion: This large case series shows that Mohs surgery results in higher rates of complete squamous cell carcinoma excision and less recurrences than excision. Therefore, Mohs surgery is an excellent treatment for high risk squamous cell carcinoma.

25. COMPARISON BETWEEN A MOBILE PHONE APPLICATION FOR THE ANALYSIS OF SKIN LESIONS AND THE CLINICAL DIAGNOSIS OF THE DERMATOLOGIST

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Objectives: To investigate the level of agreement between a mobile phone application and the dermatologist in rating skin lesions selected by patients themselves.

Methods: A Prospective clinical trial with patients who visited the pigmented lesion clinic (PLC) at the department of dermatology of the Leiden University Medical Centre for the first time were asked to point out the lesion they were worried about. Lesions were imaged by a mobile phone application prior to being diagnosed by a specialized dermatologist. The ratings of the mobile phone application were compared to the assessment of the dermatologist and, if taken, to the histological outcome.

Results: In total 151 lesions were evaluated. The measure of agreement between the ratings of the mobile phone application and the ratings of the der-
matologist was very low (weighted $\hat{P} = 0.073$).

**Conclusion:** Since the level of agreement between the ratings was very low the performance of the mobile phone application is questionable. On the one hand people might be reassured by false negative ratings which may cause delay in diagnosing skin malignancies. On the other hand, the high amount of false positive alarm might lead to increased health care consumption causing unnecessary distress and rising health costs.

### 26. Whole-Genome Sequencing Reveals Recurrent DNA Structural Alterations in Mycosis Fungoides

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**Background:** Mycosis fungoides (MF) is the most common type of Cutaneous T cell Lymphoma (CTCL), a highly heterogeneous group of extranodal non-Hodgkin Lymphomas that that first present in the skin. In MF, no recurrent point mutations have been found and only numerical alterations of broad genomic regions have been reported. This study aimed at characterizing genetic alterations in tumor-stage MF at base-resolution by employing Whole Genome Sequencing (WGS).

**Materials and Methods:** Genomic DNA from 9 tumor-stage MF biopsies was subjected to pair-end WGS on the Illumina HiSeq X-Ten platform. Raw data were processed using an in-house customized pipeline which included quality control assessment, read alignment, CNV profiling and structural variant (SV) calling. Finally, processed data were manually curated.

**Results:** The analysis of the WGS data revealed that gain of 5q14.2-telomere and 17q21.32-17q23.3, and loss of 9p21.1 (CDKN2A/B), 9q21.32 and 16p13.13 are the most recurrent copy number alterations in tumor-stage MF. All tumors except one were found to have several interchromosomal translocations (8-32), with chromosome 17 being the most frequently affected chromosome. Point mutations previously reported in CTCL were not found in our tumor samples.

**Conclusion:** Our high resolution analysis, being the first for MF, shows that alterations in narrow areas of chromosomes 5, 9, 16 and 17 appear to underlie MF development, and hitherto described point mutations in CTCL are not driving oncogenesis.

### 27. Evaluation of Validated DNA Methylation Biomarkers in Suspected Sézary Syndrome Patients

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**Introduction:** Sézary syndrome (SS) is an aggressive type of cutaneous T-cell lymphoma with a poor prognosis. Due to resembling clinical presentations and low tumor burden in peripheral blood, differentiation between SS and benign erythodermic inflammatory dermatoses (EID) is challenging, especially at early stages of the disease. Therefore, novel biomarkers are required to improve diagnostic accuracy. Recently we showed that promoter hypermethylation of PROM1, GoS2, CMTM2, C2orf40, PAM, GNMT and NEXN was frequently observed in full-blown SS patients ($T4NxMxB2$) with a diagnostic sensitivity of 80-100% and specificity of 100%.

In this study, we evaluated if promoter methylation status of these seven genes could be helpful in diagnosing patients with early stages of the disease and low tumor burden in peripheral blood.

**Methods:** Peripheral blood was drawn from 13 patients suspected for SS at stage $T4NxMxB1$ and/or $T4NxMxB0$. In order to determine the methylation status of our biomarkers panel, methylation-specific melting curve analysis (MS-MCA) was performed on DNA extracted from enriched CD4+ T-cells.

**Results:** MS-MCA showed that in 80% one or more biomarkers were hypermethylated in ten patients who had progressive disease and fulfilled WHO criteria for SS during follow-up. Patients staged $T4NxMxB1$ and $T4NxMxB0$ at least one marker was methylated in 89% and 67%, respectively. Whereas, no aberrant methylation was observed in three patients who did not develop SS during follow-up.

**Discussion:** These data suggest that testing the methylation status of this biomarker panel can be helpful in the differential diagnosis of SS and EID leading to beneficial effects on treatment and quality of life.

### 28. Results of Initial Treatment in 203 Dutch Patients with Folliculotropic Mycosis Fungoides

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**Background/Aim:** Folliculotropic mycosis fungoides (FMF) is an aggressive variant of mycosis fungoides (MF) and generally less responsive to standard skin-directed therapies (SDTs). Recent studies distinguished an indolent (early-stage FMF) and a more aggressive (advanced-stage FMF) subgroup. The optimal treatment for both subgroups needs still to be defined.

**Patients and Methods:** Evaluation of initial treatment in 203 Patients (84 early-stage, 102 advanced-stage, 17 extracutaneous FMF), included in the Dutch Cutaneous Lymphoma Registry between 1985 and 2014. Type and results of initial treatment were retrieved from the Dutch Registry. Main outcomes were complete remission (CR), sustained complete remission (SCR), partial remission (>50% improvement; PR) and overall response (OR; CR+PR).

**Results:** Patients with early-stage FMF were treated
with non-aggressive SDTs in 67 of 84 cases, resulting in CR and OR of 28% and 83% for monotherapy topical steroids, 0% and 83% for UVB and 30% and 88% for PUVA, respectively. In patients with advanced-stage FMF these SDTs were less effective (combined CR and OR: 10% and 52%, respectively). In patients with advanced-stage MFM local radiotherapy (CR 63%; OR: 100%), total skin electron beam irradiation (CR: 59%; OR: 100%) and PUVA combined with local radiotherapy (CR: 5%; OR: 75%) were most effective.

**Conclusions:** The results of the present study demonstrate that not all patients with FMF should be treated aggressively. Patients with early-stage FMF may benefit very well from standard SDTs also used in early-stage classic MF and have an excellent prognosis.

**29. STANDARD STEP SECTIONING OF SKIN BIOPSIES DIAGNOSED AS SUPERFICIAL BASAL CELL CARCINOMA FREQUENTLY YIELDS DEEPER AND MORE AGGRESSIVE SUBTYPES**

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**Background:** Correct diagnosis of superficial basal cell carcinoma (sBCC) is essential due to the increase of non-surgical treatments for this subtype. Histological confirmation by punch biopsy for the diagnosis of BCC and its subtype is recommended. However, a histological standardized method for sectioning punch biopsies is currently missing.

**Objective:** To analyze histologic combination therapy in clinical practice.

**Methods:** We collected data from five PSonet registries: Clalit Health Services (Israel), Psocare (Italy), PsorA (Austria), BioREP (Czech Republic) and AMC Medical Center Registry (the Netherlands). Data on frequency of use and patient and treatment characteristics were analyzed. Drug survival was examined using Kaplan-Meier survival analysis.

**Results:** A total of 1077 treatment cycles on biologic combination therapy were identified, accounting for 11% of total number of biologic treatment cycles registered (n=9816). Combination with methotrexate was most common (73% of biologic combinations). Combinations with UVB, acitretin and cyclosporin were prescribed in someregistries (9.7%, 9.4% and 6.1% respectively). Combination with PUVA, fumaric acid and another biologic were rare. Type and frequency of combinations used and number of prior systemic therapies varied substantially among registries. Drug survival was highest for the combinations with methotrexate and acitretin. Discontinuation of treatment due to adverse events or lack of effectiveness was low.

**Conclusions:** Biologic combination treatment is used in clinical practice in psoriasis patients.
with or without joint involvement. Combination with methotrexate is, possibly due to its positive impact on biologic pharmacokinetics, mostly used. Combination therapy with UVB and cyclosporin may be beneficial for short term. Future research is needed to examine the efficacy, safety and optimal dosing of biologic combination treatment.

**P2. WITHDRAWN**

**P3. AUTOLOGOUS CELL SUSPENSION GRATING IN SEGMENTAL VITILIGO AND PIEBALDISM: A RANDOMIZED CONTROLLED TRIAL COMPARING FULL-SURFACE AND FRACTIONAL CO2 LASER RECIPIENT SITE PREPARATIONS**

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**Background:** Autologous non-cultured cell suspension transplantation is an effective treatment for repigmentation in segmental vitiligo and piebaldism. Full surface laser ablation is frequently used to prepare the recipient site before cell suspension transplantation, even though optimal laser settings and ablation depth are unknown.

**Objective:** To assess the efficacy and safety of less invasive recipient site preparations.

**Methods:** In a randomized, observer-blinded, controlled trial we compared different recipient site preparations before cell suspension transplantation in segmental vitiligo and piebaldism. In each patient, we randomly allocated three CO2 laser recipient site preparations (i.e. 209 and 144 µm full surface, fractional) and a control (no treatment) to four depigmentations. After six months we assessed repigmentation and side effects.

**Results:** We included 10 patients with vitiligo (n=3) and piebaldism (n=7). Compared to the control site, we found more repigmentation after 209 µm (median 68.7%, p=0.01) and 144 µm (median 58.3%, p=0.007) full surface ablation, but no repigmentation after fractional ablation (median 0.0%, p=0.14). Limitations: Small number of patients and restrictions of treatment to trunk and extremities.

**Conclusion:** Superficial full surface ablation with a depth of 144 µm is an effective recipient site preparation before cell suspension transplantation while fractional CO2 laser is not.

**P4. TIGHT CONTROLLED DOSE REDUCTIONS OF BIOLOGICS IN PSORIASIS PATIENTS WITH LOW DISEASE ACTIVITY: A RANDOMIZED PRAGMATIC NON-INFERIORITY TRIAL**

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**Background:** Psoriasis is a chronic inflammatory skin disorder for which several targeted biologic therapies became available. For psoriasis patients the lowest effective dose of biologics is not known.

**Aim:** To assess whether dose tapering of biologics guided by Psoriasis Area and Severity Index (PASI) and quality of life scores in patients with controlled stable low disease activity is non-inferior (NI) to usual care.

**Methods:** A multicenter pragmatic, randomized, non-inferiority trial. One-hundred-and-twenty patients with low disease activity (PASI < 5 and DLQI ≤ 5) with stable use of adalimumab, etanercept or ustekinumab are randomized 1:1 to the dose reduction group or usual care. In the dose reduction group, treatment intervals will be increased stepwise by 1.5, followed by an increase to 2, resulting in 33 and 50% dose reduction respectively. Disease activity is monitored with PASI and DLQI. In case of flare treatment is adjusted to the previous effective dose. The primary outcome (PASI) at 12 months will be analyzed with ANCOVA. Secondary outcomes are disease flares, health-related quality of life, serious adverse events, costs and anti-drug-antibody formation.

**Results:** At present 83 patients have been included and randomized to tapering or regular care. Results will be present in the near future.

**Discussion:** With this study we want to assess whether disease activity guided dose reduction of biologics can be achieved for psoriasis patients with a low stable disease activity, without losing disease control.

**P5. THE PUTATIVE ROLE OF SKIN RESIDENT MEMORY T CELLS IN ACUTE GRAFT-VERSUS-HOST-DISEASE**

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**Background:** Graft-versus-Host-Disease (GvHD) is a major cause of illness and death in patients following hematopoietic stem cell transplantation (SCT). GvHD is assumed to result from donor-derived T cells attacking recipient tissues. However, GvHD is most common in tissues that contain large populations of long-lived resident memory T cells (TRM).

**Results:** We have found that skin resident T cells survive classic conditioning regimens including...

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**Background:** 5-10% van alle melanomen gebeuren in gezinnen met een gesloopte familie geschiedenis van melanoom. Deze patiënten worden gezien op een regelmatige basis in onze pigmentaire lesioniëres en consultatie (PLC) voor een totale lesioniërs bevinding. Meestal komen ze jaarlijks, maar soms terug voor onregelmatig bezoeken wanneer ze bezorgd zijn. 

**Aim:** Om te onderzoeken de hoeveelheid en kenmerken van patiënten met een hoge gevaar voor melanoom die terugkeren naar de PLC voor onregelmatige bijeenkomsten.

**Material / methods:** 1267 patiënten waren geïncludeerd in deze retrospectieve follow-up studie. Data werden geëxporteren in Excel, analyses werden geïmporteert in SPSS 23. 

**Results:** 110 uit 1267 patiënten haalden tenminste een interval bezoek. 31% waren man en 69% waren vrouw, met een gemiddelde leeftijd van 45 jaar. 44% van de patiënten was CDKN2A-mutatie carrier, gevolgd door de patiënten met een 50% kans van being carriers (32%), Histopathology was genomen in 59 patiënten met een gemiddelde leeftijd van 45 jaar. 44% van de patiënten was CDKN2A carrier en had meerdere melanomen in de pas. Melanomen werden ontdekt in een vroege fase. 

**Conclusion:** 9% van de hoge risico-patiënten haalden een bezoek in de tijd van de studie. Blijven weer patiënten waren van CDKN2A-mutation families. Alle melanomen waren dunne melanomen met een uitstekend overleefresultaat. Herhaald instructie voor zelf-examiniatie met de aanradings van het gebruik van een handspiegel en het gebruik van de hulp van hun partner om de melanomen te detecteren.

**P7. BOWEN’S DISEASE: FIVE-YEAR RESULTS OF TREATMENT WITH 5-FLUOROURACIL CREAM, PHOTODYNAMIC THERAPY AND SURGICAL EXCISION**

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**Background/Aim:** Excoriërende behandeling (SE) en enkele topische therapieën (bijv. photodynamische therapie (PDT), 5-fluorouracil (5-FU)) zijn bevaat behandelingen voor Bowen’s disease (BD), maar recente richtlijnen bevestigen dat geen van deze behandelingen een betere is. Huidliteratuur over niet-invasieve behandelingen voor BD is zeldzaam en de meeste studies zijn klein in omvang. Deze studie heeft de efficiëntie van SE en PDT in vergelijking met BD gemeten.

**Materials and Methods:** Eligible for inclusion were patients with a histologically proven BD in the period from January 2008 until December 2013. Data were retrospectively collected by reviewing patient medical and histological records. Patients treated with 5-FU, SE or PDT were compared in terms of five-year cumulative probability of treatment failure. 

**Results:** A total of 841 BD lesions in 608 patients were identified. PDT was used in 450 lesions (53.5%), SE in 246 (27.5%), 5-FU in 72 (8.6%) and other treatments in 31 (3.7%) lesions. Median follow-up was 8 months (range 0-87 months). After correction for confounders, the 5-year probability of treatment failure was twice as high after treatment with 5-FU (HR 2.22, 95% CI 0.98-5.04) and PDT (HR 2.71, 95% CI 1.52-4.83) when compared to SE. Probability of treatment failure in the 5-FU group was similar to the PDT group (adjusted HR 1.22, 95% CI 0.62-2.41).

**Discussion/Conclusion:** Our study showed that SE is associated with the lowest 5-year probability of treatment failure post treatment compared to PDT and 5-FU. No significant difference in treatment failure between 5-FU and PDT was found.

**P8. TOPICAL SINECATECHIN OINTMENT FOR PRIMARY SUPERFICIAL BASAL CELL CARCINOMA: CAN TEA CURE? RESULTS FROM A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL**

Background/Aim: Topical Sinecatechins 10% (Veregen®) ointment is known for its anti-viral properties, anti-proliferative effects and induction of apoptosis. It is suggested that the active constituent ß-EGCG - ß-GC0 has anti-tumoral effects. We aimed to assess whether topical Sinecatechins 10% ointment could lead to histological clearance of sBCC. Secondly we assessed the proportion of patients with decreased immunohistochemic expression of Ki-67 and Bcl-2.

Materials and Methods: We performed a single center, double blind, randomized, placebo-controlled clinical trial. 42 patients were assigned to Sinecatechins or placebo ointment and instructed to apply the ointment twice daily during 6 weeks. All tumors were removed by surgical excision after 8 weeks.

Results: Complete histological tumor clearance was seen in 12/21 (48.8%) and 2/21 (9.5%) patients of the Sinecatechins and placebo group respectively (p = 1.000). Decrease in Bcl-2 expression was observed slightly more frequently in the Sinecatechins 10% group than in the placebo group (respectively 41.2% vs 23.5%, p = 0.163) and decrease in Ki-67 occurred in similar proportions in both groups (31.3% versus 29.4%, p = 0.909). Most local skin reactions occurred in the Sinecatechins 10% group in the fourth week of treatment.

Discussion/Conclusion: Based on these study results, there are insufficient grounds to further explore topical Sinecatechins 10% ointment for treatment of sBCC. This trial is registered on clinicaltrials.gov (NCT02029352).

P10. SICKNESS PRESENTEEISM IN A DUTCH HAND ECZEMA POPULATION

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Background: Sickness presenteeism (SP, attending work despite being ill) can cause increased health problems and might be associated with sickness absenteeism in the long-term. Also, continuous work impairment due to SP could eventually cause even more aggregate productivity loss than sickness absenteeism.

Objective: To examine the extent of and reasons for SP - as measured by the person’s own assessment of their state of health - and to investigate the associations between HE severity, work characteristics, demographic factors and SP in patients with HE.

Method: Questionnaire-based (postal and on-site), cross-sectional study. The study population consisted of adults (age 20-67) with a dermatologists diagnosis of HE, made in the past 5 years, added to a group of new, on-site recruited patients. Severity was assessed using a self-administered photoguide. Associations were studied using binomial logistic regression.

Results: Valid response rate was 46.0% (320/789). 30 additional patients were included on-site. 233 patients proved eligible for analysis (working with HE in the past 12 months). SP was present in 38.6%. It was associated with moderate and severe HE; sickness absenteeism; improvement of HE when away from work; and exposure at work aggravating HE. Not just extrinsic, but also intrinsic reasons were found for SP.
Conclusion: SP is common in HE and is significantly associated with work factors. Dermatologists should make patients aware of the risks of this potentially negative behavior (particularly when reasons for SP are intrinsic) and encourage them to contact an occupational physician for implementation of secondary preventive measures.

P11. IN VITRO KERATINOCYTES BINDING TEST FOR PEMPHIGUS

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The serological diagnosis of pemphigus relies on the detection of IgG autoantibodies directed against the epithelial cell surface (ECS) by indirect immunofluorescence on monkey oesophagus and against desmogleins 1 and 3 (Dsg1 and Dsg3) by ELISA. Although ELISA has a high sensitivity and even higher specificity, we detected anti-Dsg1 and/or anti-Dsg3 IgG by ELISA in a number of patients with negative indirect immunofluorescence and who were not affected by pemphigus. Therefore, we designed and validated a new serological test to determine whether anti-Dsg1/3 IgG detected by ELISA are actually able to bind in a specific desmosomal pattern by living keratinocytes. The in vitro keratinocytes binding test we propose, uses cultured primary normal human keratinocytes, grown under different conditions so to induce adequate expression of Dsg1 and/or Dsg3, subsequently incubated with the selected patient serum for one hour. The immunostaining for human IgG of pemphigus patient sera on keratinocytes revealed a characteristic desmosomal pattern and IgG internalization, while the sera of the non-pemphigus patients showed no binding, confirming that some positive ELISA results were false, thus preventing misdiagnosis.

P12. VASCULAR MALFORMATIONS OF SOFT TISSUE: CLINICAL VERSUS HISTOLOGIC DIAGNOSIS

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Background: The classification of vascular anomalies, established by the International Society for the Study of Vascular Anomalies (ISSVA), is used for guidance in the diagnosis of soft tissue vascular malformations. Although this classification is partially based on histopathologic features, diagnostic histologic examination is not routinely performed in practice. In order to evaluate the validity of the current diagnostic process, we determined if clinical diagnoses corresponded with histopathologic diagnoses in patients with vascular malformations undergoing non-diagnostic surgical resections.

Methods: Clinical data and histology reports from patients undergoing surgery in our center between 2000 and 2015 were retrospectively collected. An experienced pathologist performed blinded revision of the initial tissue samples according to the ISSVA classification.

Results: In 55.2% of a total of 143 cases, there were discrepancies between clinical and the unrevised histological diagnoses. This was caused by inaccurate terminology in 8.9%. However, after histology revision using the ISSVA terminology, there were even more discrepancies between the clinical and the revision histological diagnoses (57.3%). A large percentage of discrepant diagnoses were found in relation to combined vascular malformations (18.7%). Proper immunostaining (e.g. D2-40), necessary for diagnosing subtypes, was missing in the majority of cases.

Conclusions: Although the ISSVA classification has cleared the majority of nomenclature issues, clinicians and pathologists still do not agree on the diagnosis in more than half of patients with vascular malformations. Clinicians and pathologists have to work together to develop clear clinical and histopathologic criteria for the diagnosis of vascular malformations, in addition to the existing ISSVA classification.

P13. DETERMINANTS FOR DRUG SURVIVAL OF METHOTREXATE IN PATIENTS WITH PSORIASIS, SPLIT FOR DIFFERENT REASONS OF DISCONTINUATION - RESULTS OF THE PROSPECTIVE MTX-CAPTURE

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Background: Methotrexate is a widely used treatment for psoriasis. It is important to gain insight into the reasons for discontinuation of methotrexate and determinants for drug survival.

Objectives: To describe 5-year drug survival for methotrexate in patients with psoriasis split for different reasons of discontinuation, and to identify determinants for drug survival.

Conclusion: SP is common in HE and is significantly associated with work factors. Dermatologists should make patients aware of the risks of this potentially negative behavior (particularly when reasons for SP are intrinsic) and encourage them to contact an occupational physician for implementation of secondary preventive measures.
Methods: Data were extracted from a prospective psoriasis registry of patients treated with methotrexate (MTX-CAPTURE). Drug survival was analyzed using Kaplan-Meier estimates and determinants for discontinuation were analyzed using Cox-regression analysis. Analyses were split for reason of discontinuation: side effects or ineffectiveness.

Results: We included 85 patients treated with methotrexate with a maximum treatment duration of 5.2 years. The overall drug survival rates were 62.7%, 30.1%, and 15.1% after 1, 3, and 5 years, respectively. The median survival was 1.8 years. Fifty-five patients (64.7%) discontinued MTX; reasons were: side effects (34.5%), ineffectiveness (25.5%), combination of side effects and ineffectiveness (12.7%), other reasons (16.4%), and lost to follow-up (10.9%). Most reported side effects were gastrointestinal symptoms, despite folic acid use in 99% of patients. Based on univariate analysis, a high Psoriasis Area and Severity Index and Visual Analogue Scale for disease severity at baseline were possible determinants for a short drug survival.

Conclusion: drug survival of MTX was low with 15% of patients ‘on drug’ after 5 years. Side effects alone or in combination with inadequate disease control were more important in the context of treatment discontinuation than inadequate disease control solely.

P14. PREDICTING THE RESPONSE TO BIOLOGICS IN PATIENTS WITH PSORIASIS THROUGH PHARMACOGENETICS: A SYSTEMATIC REVIEW

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Background: The response to biologics among psoriasis patients is heterogeneous. As the number of biologics registered for psoriasis increases, so does the need for biomarkers to guide personalized therapeutic decisions. Genetic variants might serve as such predictors for treatment response, a field of research known as pharmacogenetics.

Aim: We aimed to accumulate the existing evidence regarding genetic variation as a predictive tool for therapeutic efficacy in psoriasis patients treated with biologics, and to evaluate the current clinical applicability of this evidence.

Materials and methods: We carried out a systematic literature search in EMBASE, MEDLINE, the Cochrane Library and Web of Science. Article screening and selection was performed independently by two reviewers. Quality assessment was performed for all included papers.

Results: Twenty-six papers were included in the systematic review. Studied biologics were adalimumab, etanercept, infliximab and ustekinumab. No studies on secukinumab or ixekizumab were identified. The majority of studies were based on a candidate gene approach, focusing on psoriasis susceptibility genes such as HLA-Cw6. Tumour necrosis factor inhibitors were analyzed as a group in most papers. The genetic associations discovered in these studies were weak and often irreproducible.

Conclusion: Pharmacogenetics research in psoriasis has produced inconclusive results. No genetic variant with sufficient predictive potential to be used in daily practice has been identified so far. We believe that large genome-wide association studies are needed to allow a hypothesis-free search for genetic biomarkers. Extensive projects like this can only be realized through international collaborations, uniting psoriasis cohorts into large consortia.

P15. MIXTURUSED IN PERMANENT HAIR DYES ENHANCES TOXIC EFFECTS IN RECONSTRUCTED 3D EPIDERMAL EQUIVALENTS: ROLE OF P-PHENYLENEDIAMINE, BARRIER LOSS AND SKIN SENSITIZATION

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Skin is a frequent target of allergic and irritant reactions caused by topical exposure of permanent hair dyes. These hair dyes are formed by a mixture of ingredients that vary from low to extreme skin sensitizers that react among themselves forming unknown by-products. The specific allergic mechanism of these mixtures has not yet been elucidated. Reconstructed epidermal models could be a useful tool to predict the skin sensitization potential of these dyes and their mixtures as they allow the evaluation of some parameters involved in skin allergy. A reconstructed epidermal equivalent (EE) that structurally and functionally resembles native human epidermis was topically exposed to p-phenylenediamine (PPD), Resorcinol (RES), H2O2 alone or a combination. Next some parameters involved in skin allergy such as epidermal viability, barrier loss, and IL-1α and IL-1β were evaluated. Here, we evaluate some parameters involved in the allergic potential of PPD, RES, H2O2 alone and in combination. Our data indicates that when the ingredients were tested alone no morphological changes were observed in EE although after exposure to the mixture of PPD/H2O2/RES and PPD/H2O2 some events such as morphological changes, barrier loss, apoptotic cells increase followed by increase of IL-1α and IL-1β were observed. Our results suggest that the allergic potential of these mixtures are complex mechanisms which require further investigation. Mixtures of the ingredients used in permanent
Hair dye formulations enhances some parameters involved in skin allergy induction. Therefore, the formation of some unknown by-products could be the key of skin allergic induction by hair dyes and should be better investigated.

P16. IMPROVEMENT OF BARIER PROPERTIES IN HUMAN SKIN EQUIVALENTS

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Skin equivalents (HSE) are human skin models generated from fibroblasts and keratinocytes, both isolated from native human skin (NH). Although many characteristics are similar to those of NH, the skin barrier function of these HSEs is impaired compared to NH. In recent studies it was shown that the lipid composition in stratum corneum (SC) deviates from that in NH, especially the high level of unsaturated fatty acids (MUFA). This may explain the impaired skin barrier. The aim of this study is to synthesize and characterize SC models from human skin sensory tissues.

COSentyx 150 mg oplossing voor injectie bij plaque psoriasis

Cosentyx is een geneesmiddel dat te worden gebruikt bij volwassenen met matige tot ernstige plaque psoriasis. Het geneesmiddel wordt gebruikt als een ondersteunende behandeling van secukinumab. Elke voorgevulde pen bevat 150 mg secukinumab in 1 ml. Deze formule is alleen te gebruiken bij patiënten met matige tot ernstige plaque psoriasis. Bij patiënten met een chronische ziekte van Crohn, diabetes mellitus type 1, longontsteking, andere auto-immuunziekten of een reactie tegen secukinumab, moet Cosentyx niet worden gebruikt.

Cosentyx is geïndiceerd voor de behandeling van platelet psoriasis bij volwassenen die in aanmerking komen voor een andere systemische behandeling, zoals cyclosporine, methotrexaat of PUVA/UVB. Bij patiënten met een voorgeschiedenis van depressie, moet de toediening van Cosentyx worden onderbroken en de voorschriften van de behandelingsaanpak onderbroken worden. Bij patiënten met allergies of voor eerdere DMARD-therapie, is geïndiceerd voor de behandeling van actieve arthritis psoriatica bij volwassen patiënten die een onvoldoende respons hebben vertoond op of intolerant waren voor een eerdere DMARD-therapie.

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